Preexisting Cognitive Impairment and Mild Cognitive Impairment in Subjects Presenting for Total Hip Joint Replacement

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ABSTRACT

Background: The prevalence of preexisting cognitive impairment (PreCI) is documented before cardiac surgery, but there is less information before noncardiac surgery. In addition, the prevalence of mild cognitive impairment, defined by different cognitive criteria and subjective complaints, and which may progress to Alzheimer disease, is unknown in these subjects. Because anesthesia and surgery have been implicated in Alzheimer disease pathology, we prospectively measured PreCI and mild cognitive impairment in subjects scheduled for total hip joint replacement surgery in an observational study.

Methods: One hundred fifty-two subjects 60 y of age and older who were scheduled for total hip joint replacement surgery underwent assessment, including neuropsychologic testing, 1 week before surgery. Test results were compared with published norms. PreCI was defined as impairment in two or more of seven cognitive tests, for which impairment in an individual test was defined as ≥2 SD below norms for that test. Amnestic mild cognitive impairment (aMCI) was defined as impairment ≥1.5 SD below norms for results of the immediate and/or delayed Auditory Verbal Learning Test plus a subjective complaint.

Results: Subjects performed worse compared with normative data on five of seven neuropsychologic tests. Thirty (20% [95% CI, 13–26%]) subjects were classified as having PreCI. Thirty-four (22% [95% CI, 16–29%]) were classified as having aMCI. Ten (7%) subjects were classified as having both PreCI and aMCI, representing 33% of the 30 subjects with PreCI.

Conclusions: The prevalence of aMCI in subjects scheduled for total hip joint replacement surgery is similar to that in the general community. PreCI and aMCI tend to identify different subjects. Because aMCI is known to progress to Alzheimer disease, future studies that track cognition before and after anesthesia and surgery should document the presence or absence of aMCI so that the rate of conversion to Alzheimer disease after anesthesia and surgery can be compared with the rate in the nonsurgical population.

What We Already Know about This Topic

- The prevalence of preexisting cognitive impairment (PreCI) and amnestic mild cognitive impairment (aMCI), which is known to progress to Alzheimer disease, is poorly characterized before noncardiac surgery but could be used to compare disease progression in patients who undergo such surgery and those who do not.

What This Article Tells Us That Is New

- Elderly subjects presenting for elective total hip joint replacement surgery exhibit PreCI (20%) and aMCI (22%), the latter being similar to that of aged individuals in the wider community. PreCI and aMCI tended to identify different subjects.

POSTOPERATIVE cognitive dysfunction (POCD) refers to a measurable decline in cognitive function detected by neuropsychologic testing before and after anesthe-

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sia and surgery. Studies by Moller *et al.*[1] and Monk *et al.*[2] documented objective evidence of POCD at 3 months after noncardiac anesthesia and surgery in 9.9% and 12.7% of elderly subjects, respectively. Although it is acknowledged that the incidence of POCD increases with age, the exact cause remains unknown.

Attribution of POCD requires measurement of cognition at a preoperative time point to establish a baseline level from which change can be calculated.[3] This is an important measurement because any subsequent calculation of change is dependent on the initial baseline assessment. Furthermore, preoperative baseline testing determines whether subjects presenting for surgery exhibit cognition within normal limits or if they exhibit cognitive function that is different from that of seemingly normal individuals who do not require surgery. These determinations have been made in subjects presenting for coronary artery bypass (CABG) surgery. Hogue *et al.*[4] found that 45% of women presenting for CABG surgery exhibited preexisting cognitive impairment (PreCI) and Silbert *et al.*[5] showed that PreCI was present in 35% of subjects before elective CABG surgery. These high rates of baseline cognitive impairment were attributed to cardiovascular disease, which had led the subjects to present for CABG surgery. Given that cardiovascular disease or risk factors for cardiovascular disease are known to be associated with cognitive impairment,[6,7] it is not surprising that many subjects presenting for CABG surgery have impaired cognition.

Coronary artery bypass surgery accounts for less than 1% of surgery undertaken in Australia every year. Thus, it is germane to establish the prevalence of PreCI in subjects undergoing noncardiac surgery, such as orthopedic surgery. This will highlight the importance of baseline cognition in calculating POCD in all subjects and identify the number of subjects presenting for surgery with impaired cognition. Identifying subjects with impaired cognition raises methodological issues between the anesthetic literature and the psychogeriatric literature because the two streams of research have taken differing approaches to assessing cognitive impairment. Previous studies of cognition in subjects presenting for anesthesia and surgery have defined PreCI using strict objective criteria. Studies in the psychogeriatric literature have focused on mild cognitive impairment (MCI), a construct defined when (1) the subject is neither normal nor demented; (2) there is evidence of cognitive deterioration shown by objectively demonstrable cognitive deficits and a subjective report of decline or an equivalent report from an informant (amnestic MCI [aMCI] is characterized by decline in memory either alone or in conjunction with other domains); and (3) activities of daily living are preserved with complex instrumental functions intact or minimally impaired.[8]

Subjects classified as having aMCI experience conversion to Alzheimer disease (AD) at a rate of 10–15% per year, compared with age-matched controls without aMCI, who experience conversion to AD at 1–2% per year.[9] Most research within the field of anesthesia has classified cognition using strict objective criteria (*e.g.*, ≥2 SD below controls on two or more of seven or eight neuropsychologic tests[4,5]) compared with the psychogeriatric literature, which has usually used less conservative criteria (*e.g.*, ≥1.5 SD below controls in memory testing alone). In addition, the failure to record reports of subjective complaints of memory deterioration has excluded anesthesia research from evaluating subjects for the presence of aMCI because this essential element of the definition has been lacking. This has become problematic as recent laboratory evidence has implicated anesthesia in the pathogenesis of AD,[10,11] although at this time, a clinical association has not been identified. In an attempt to link the two constructs, some authors have attempted to classify retrospectively subjects with aMCI by using the scores from memory testing, but the lack of subjective reports by the subjects or informants has made classification of aMCI impossible.[12]

We therefore aimed to define prospectively the prevalence of PreCI and aMCI in a group of subjects presenting for elective total hip joint replacement (THJR) surgery. Documentation of this data would establish the prevalence of PreCI and aMCI in subjects undergoing THJR surgery and identify factors associated with the presence of these two constructs. It would also relate the anesthetic concept of PreCI with the neuropsychiatric concept of MCI. In addition, because the rate of conversion of aMCI to AD is known, some indication of the expected onset of AD in the absence of anesthesia and surgery could be ascertained.

Materials and Methods

The data were prospectively collected as part of the Anesthesia Cognition Evaluation Study, which was designed to assess cognition in subjects scheduled for elective THJR. The study was approved by the St. Vincent's Hospital Research Ethics Committee (Melbourne, Victoria, Australia), and all subjects provided written informed consent. Inclusion criteria were subjects older than 60 y presenting for elective THJR for osteoarthritis, with no neurologic deficit and no contraindication to neuropsychologic testing. The subjects resided in accessible proximity to the hospital to enable investigators to administer baseline neuropsychologic testing at the subjects' home. Exclusion criteria were preexisting neurologic or clinically evident neurovascular disease (*e.g.*, stroke), Mini–Mental State Examination score of less than 26 or Clinical Dementia Rating[13] ≥1 (*i.e.*, frank dementia excluded), anticipated difficulty with neuropsychologic assessment (*e.g.*, English not being the prime language, blindness, deafness), and medical problems that might lead to significant complications resulting in subsequent loss to follow-up (American Society of Anesthesiologists Physical Status 4 or higher).

To assess cognition in these subjects scheduled for THJR surgery, results were compared with previously published normative data for each test.

Assessment of Subjects

The neuropsychologic tests used in this study were selected on the basis of their sensitivity to impairment in a range of cognitive domains in older people and met previously recommended criteria.[14] The test battery consisted of the Consortium to Establish a Registry for Alzheimer's Disease Auditory Verbal Learning Test (CERAD AVLT) (immediate and delayed recall), Trail-making Test parts A and B, Controlled Oral Word Association Test, semantic fluency (CERAD animal naming), and the Grooved Pegboard Test (dominant and nondominant). All of these tests have been described elsewhere.[15] The results are given as the number of correct answers or the time taken to complete the test. Intelligence quotient was derived from the results of the National Adult Reading Test,[16] which incorporates the number of years of education.

All neuropsychologic assessments were conducted by trained assessors and were conducted under the supervision of a neuropsychologist (P.M.). Attempts were made to keep the environment comfortable and free of distractions.

The presence of anxiety, depression, fatigue, and pain may affect the performance of cognitive testing; thus, visual analog scales were used to assess each of these at the time of testing. Visual analog scales are especially suitable for this situation because they offer simple, reliable, and valid techniques while placing minimal demands on subjects.[17,18] Subjects were asked to mark an ungraded line (10 cm in length) anchored by "least" and "most" at each end.

Subjective decline in cognition was assessed by asking subjects "are you having trouble with your memory in everyday life?" and from informants by the response to the memory question "does he/she have a problem with memory or thinking?" in the Clinical Dementia Rating.[13] Changes in activities of daily living were reported by both subject and informant on the Clinical Dementia Rating.

Classification of PreCI and MCI

Performance on each test was standardized to z scores using the mean and SD of published normative data.[19–21]** The signs of the standardized scores were adjusted for all measures so that negative scores indicated poorer performance. Subjects were classified as having PreCI using the definition of Hogue *et al.*[4] if they scored ≥2 SD below norms on two or more of the seven neuropsychologic tests. Using binomial distributions and assuming the hypothesis is one-tailed, the probability of type 1 error using this criterion for a battery of seven tests is less than 5%.[3,22] For CERAD AVLT the immediate recall score for each of the three trials was used (total score possible for each trial was 10). A subject was classified as having a deficit for this test when the result was ≥2 SD below norms on at least two of the three trials.

For aMCI, subjects were deemed to have objective decline in cognitive function when their score in the CERAD AVLT immediate and/or delayed was ≥1.5 SD below norms (≥2 of 3 trials).[23] In addition, to satisfy the definition of aMCI there had to be a subjective complaint of cognitive decline by the subject or a positive response by the informant on the Clinical Dementia Rating questionnaire.

Data Analysis

Group comparisons were made using independent *t* tests for continuous variables, Mann–Whitney U test for ranked data, and chi-square or Fisher exact test for dichotomous parameters. Effect size was calculated using Cohen's d (*d* is defined as the difference between two means divided by the pooled SD for those means).[24]

Associations were determined using univariable and multivariable regression with a $P < 0.2$ set for entry into multivariable regression. Seven cardiovascular risk factors (body mass index, diabetes, hypertension, peripheral vascular disease, history of myocardial infarction, smoking [current or previous], and hypercholesterolemia) (table 1) were summed to create a single variable to quantify total cardiovascular risk. Tests were performed using STATA (Version 11.0; StataCorp, College Station, TX). A $P < 0.05$ was taken to indicate statistical significance. All analyses were two-tailed comparisons.

Results

The subject characteristics, including medical history and medications, are shown in table 1.

Table 1. Subject Demographics and Medical History

—	n	—
Age, y	152	69.8 (6.3)
Gender (M/F)	152	54/98
Height, cm	149	166.4 (9.3)
Weight, kg	150	78.6 (14.6)
Body mass index*	149	28.5 (4.9)
Diabetes*	149	13 (9%)
Hypertension*	150	79 (53%)
Peripheral vascular disease*	140	1 (1%)
History of myocardial infarct*	148	7 (5%)
Smoking (current or previous)*	150	72 (48%)
Hypercholesterolemia*	149	52 (35%)
Estimated IQ	137	110.9 (9.7)
Preoperative medications	—	—
Analgesics	151	29 (19%)
Paracetamol	151	48 (32%)
NSAIDs	151	50 (33%)
ACE inhibitors	151	30 (20%)
Statins	151	45 (30%)
β blockers	151	16 (11%)
Antidepressants	148	14 (9%)

Continuous variables are presented as mean (SD), and categorical variables are presented as frequency (percentage). Although 152 subjects were studied, data were not collected or were missing for some, accounting for the discrepancy in numbers of subjects for some variables.

* Included in total cardiovascular risk sum score.

ACE = angiotensin-converting enzyme; IQ = intelligence quotient; NSAIDs = nonsteroidal antiinflammatory drugs.

** Lafayette Instrument. Grooved Pegboard Test (model 32025). www.lafayetteinstrument.com. Accessed November 24, 2010.

Table 2. Neuropsychologic Test Results, Subjects, and Published Norm Values

Test	Subjects (n = 152)		Published Norm Values		Effect Size (Cohen's d)
	Completing Tests (n)	—	Completing Tests (n)	—	—
CERAD AVLT	—	—	—	—	—
Immediate, n	—	—	—	—	—
<12 y education <69y*	48	7.0 (1.4)	23	8.1 (1.3)	0.82
<12 y education ≥70y*	50	6.2 (1.6)	23	7.6 (1.9)	0.84
≥12 y education, males <69 y	11	7.7 (1.1)	61	8.0 (1.3)	0.24
≥12 y education, males ≥70 y*	6	4.8 (1.5)	66	7.7 (1.5)	1.96
≥12 y education, females <69 y*	23	7.1 (1.6)	151	8.8 (1.0)	1.56
≥12 y education, females ≥70 y*	14	6.9 (1.7)	89	8.2 (1.4)	0.91
Delayed, n	—	—	—	—	—
<12 y education <69 y*	48	4.7 (2.1)	23	7.0 (1.9)	1.14
<12 y education ≥70 y*	50	4.2 (2.3)	23	6.7 (1.9)	1.16
≥12 y education, males <69 y*	11	4.2 (2.1)	61	7.0 (2.1)	1.35
≥12 y education, males ≥70 y*	6	1.8 (1.6)	66	6.3 (1.8)	2.55
≥12 y education, females <69 y*	23	4.5 (2.0)	151	7.9 (1.6)	2.06
≥12 y education, females ≥70 y*	14	4.3 (2.1)	89	6.9 (1.7)	1.49
TMTA,* s	149	53.2 (23.5)	156	48.7 (14.5)	0.23
TMTB,* s	147	121.3 (68.4)	156	107.6 (45.6)	0.24
COWAT, n	—	—	—	—	—
Age <70 y	82	35.3 (13.1)	220	38.5 (13.7)	0.24
Age 70–79 y	59	34.1 (12.0)	334	34.8 (12.8)	0.06
Age ≥80 y	11	32.8 (11.9)	200	28.9 (11.7)	0.33
CERAD fluency, n	—	—	—	—	—
Age <70 y	82	18.4 (4.9)	92	17.6 (4.7)	0.17
Age 70–79 y	59	17.0 (4.1)	228	16.1 (4.0)	0.22
Age ≥80 y	11	14.6 (4.7)	200	14.3 (3.9)	0.08
GPD,* s	150	100.0 (41.9)	100	82.7 (18.7)	0.50
GPND, s	149	111.0 (48.3)	100	87.9 (26.2)	0.57

Test results are either number correct (n) or time taken (s). Data are presented as mean (SD).

* $P < 0.05$.

CERAD AVLT = Consortium to Establish a Registry for Alzheimer's Disease Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; DSST = Digit Symbol Substitution Test; GPD = Grooved Pegboard Test, Dominant; GPND = Grooved Pegboard Test, Nondominant; TMTA = Trail-making Test Part A; TMTB = Trail-making Test Part B.

One hundred fifty-two subjects underwent neuropsychologic testing. Subjects performed worse compared with normative data on five of the seven neuropsychologic tests. Group mean scores on neuropsychologic tests and effect size (Cohen's d) are shown in table 2. Cohen's d indicates that the difference between subjects and norms was large for CERAD AVLT (immediate and delayed), medium for Grooved Pegboard Test (dominant and nondominant), and small for Trail-making Test (parts A and B).

The number and percentage of impaired performances in each individual test are shown in table 3. Thirty (20% [95% CI, 13–26%]) subjects satisfied the criteria for PreCI (impairment in two or more of the seven tests). The prevalence of PreCI was more common in older individuals (60–69 y: 8 of 82 [10%]; 70–79 y: 16 of 59 [27%]; ≥80 y: 6 of 11 [55%]; chi-square = 15.6, $P < 0.001$).

The number and percentage of subjects who satisfied the objective criteria for aMCI (≥1.5 SD below controls on the CERAD AVLT, immediate and/or delayed) was 76 (50% [95% CI, 42–58%]). This consisted of 57 of 152 (38%) who failed the delayed recall, 17 of 152 (11%) who failed both memory components, and 2 of 152 (1%) who failed the immediate recall only. When the qualifying requirement for aMCI of subjective complaint by the subject or informant was added, 34 (22% [95% CI, 16–29%]) were classified as having aMCI. The prevalence of aMCI was not associated with age (≤69 y: 18 of 82 [22%]; 70–79 y: 13 of 59 [22%]; ≥80 y: 3 of 11 [27%]; chi-square = 0.2, $P = 0.92$).

No subjects or informants reported changes in activities of daily living.

When examining cognition alone, 21 of the 30 subjects with PreCI (70%) met objective cognitive criteria for aMCI (chi-square = 5.98; $P = 0.01$) (fig. 1). When the subjective component was included, 11 of the 21 subjects did not qualify for aMCI classification, leaving only 10 of the 30 subjects (33%) with a dual classification. The relationship between subjects with PreCI and aMCI is shown in figure 2. PreCI was not associated with aMCI (chi-square = 2.59, $P < 0.11$).

For PreCI, multivariable logistic regression showed associations with age and pain, whereas for aMCI, depression and total cardiovascular risk were associated (table 4).

Table 3. Neuropsychologic Tests Classifying Preexisting Cognitive Impairment

Test	Completing Tests (n)	Impaired Performance n (%)
CERAD AVLT, n	152	11 (7%)
TMTA, s	149	22 (15%)
TMTB, s	147	16 (11%)
COWAT, n	152	2 (1%)
CERAD fluency, n	152	2 (1%)
GPD, s	150	22 (15%)
GPND, s	149	24 (16%)

Impaired performance presented as frequency (percentage).

CERAD AVLT = Consortium to Establish a Registry for Alzheimer's Disease Auditory Verbal Learning Test; CERAD fluency = CERAD semantic fluency, animal naming; COWAT = Controlled Oral Word Association Test; GPD = Grooved Pegboard Test Dominant; GPND = Grooved Pegboard Test, Nondominant; TMTA = Trail-making Test Part A; TMTB = Trail-making Test Part B.

Discussion

The measurement of cognition in elderly subjects scheduled to undergo THJR surgery and anesthesia is important because preoperative cognition may be highly relevant in determining long-term cognitive outcome. Previous studies have identified a prevalence of PreCI in 45% and 35% of subjects undergoing elective CABG surgery,[4,5] but there is little information on prevalence before THJR surgery. We determined this prevalence by two distinct approaches. The first method used strict objective criteria, as has been used before CABG surgery, to classify PreCI. Using this approach, PreCI was identified in 20% of subjects. The second method used a technique routinely used to classify aMCI. This method required a much less stringent criterion for objective change (≥1.5 SD below controls on CERAD AVLT, immediate and/or delayed recall) plus a subjective or informant cognitive complaint. Using this approach, 22% of subjects were classified as having aMCI. Only 10 of 152 (7%) subjects satisfied a classification for both aMCI and PreCI.

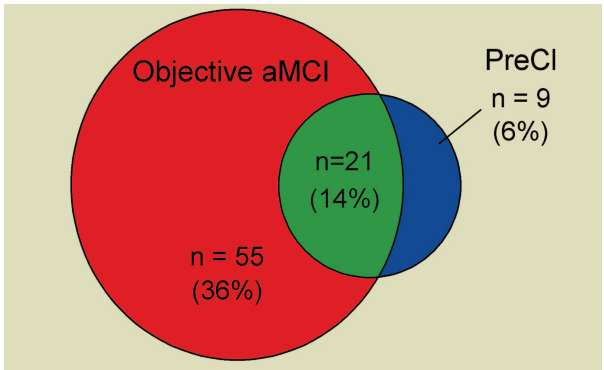

Fig. 1. Subjects who qualified for the objective criteria for amnestic mild cognitive impairment (aMCI) (more than 1.5 SD decline on immediate and/or delayed Consortium to Establish a Registry for Alzheimer's Disease Auditory Verbal Learning Test), subjects who qualified for preoperative cognitive impairment (PreCI) (more than 2 SD decline in two of seven neuropsychologic tests), and those who satisfied both requirements.

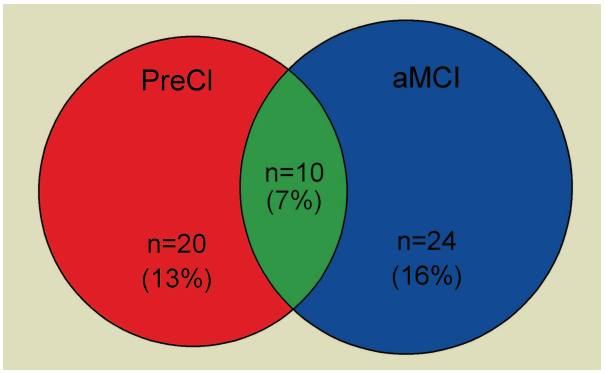

Fig. 2. Subjects who were classified as having amnestic mild cognitive impairment (aMCI), preoperative cognitive impairment (PreCI), or both.

The prevalence of PreCI of 20% in subjects presenting for THJR surgery is less than the reported prevalence before CABG surgery. This may be attributed to the higher presence of cardiovascular risk factors present in subjects presenting for CABG surgery; cardiovascular disease and risk factors for it are known to be associated with cognitive impairment.[5]

Several components account for the variation in prevalence between PreCI and aMCI. First, the definition of PreCI incorporates several cognitive domains other than memory; second, PreCI uses only immediate recall and not delayed recall; third, the statistical thresholds are more conservative; and finally, no subjective complaint is required. Incorporating MCI of the nonamnestic type would increase the prevalence of MCI, but this type of MCI, although it may progress to dementia, is thought to progress to non-AD dementia[25] and thus may be of less interest in the context of AD risk with anesthesia and surgery.

Perhaps the greatest discrepancy between the two constructs lies in the failure to incorporate subjective complaints into the definition of PreCI. Seventy percent of subjects with PreCI satisfied the objective criteria for aMCI, but when a subjective complaint was incorporated into the definition of aMCI, the number fell to 30%. Although some published studies have failed to include memory complaints as a criterion for aMCI,[26] there is evidence that subjective memory complaint is an important component of MCI.[27] To align studies of cognition with the field of psychogeriatrics, the inclusion of subjective changes should be documented. In this manner, conversion rates to AD after anesthesia can be compared with population studies. This would give some insight into the effect of anesthesia and surgery on the rate of conversion of MCI to AD.

A variety of methods have been used to assess the presence of MCI in different settings, (*e.g.*, population based *vs.* clinical), and this undoubtedly accounts for variations in prevalence.[25] The method used in the current study (1.5 SD below normative values on memory testing together with memory

Table 4. Univariable and Multivariable Analyses

Predictor	Univariable Analysis		Multivariable Analysis	
—	—	*P* Value	Odds Ratio [95% CI]	*P* Value
Pre-existing cognitive impairment		—	—	—
Age	t = −4.855	<0.001	1.17 [1.07, 1.29]	0.001
Intelligence quotient	t = 2.773	0.006	0.94 [0.88, 1.00]	0.058
Pain	t = −1.955	0.053	1.03 [1.01, 1.04]	0.010
Statins	Chi-square = 1.719	0.190	0.38 [0.09, 1.49]	0.164
Anxiety	Chi-square = 1.793	0.075	0.98 [0.96, 1.00]	0.063
Mild cognitive impairment			—	
Anxiety	t = −1.336	0.183	1.01 [0.99, 1.03]	0.299
Depression	t = −1.969	0.051	1.02 [1.00, 1.04]	0.018
Smoking*	Chi-square = 2.064	0.151	1.67 [0.74, 3.82]	0.217
Hypercholesterolemia*	Chi-square = 3.443	0.064	2.21 [0.96, 5.08]	0.062
Paracetamol	Chi-square = 1.784	0.182	1.32 [0.53, 3.25]	0.548
NSAIDs	Chi-square = 1.820	0.177	0.71 [0.28, 1.82]	0.480
Total cardiovascular risk	r = 0.150	0.080	1.52 [1.06, 2.18]	0.024

Total cardiovascular risk includes the sum of body mass index, diabetes, hypertension, peripheral vascular disease, history of myocardial infarction, smoking (current or previous), and hypercholesterolemia.

* Smoking and hypercholesterolemia are included in the variable total cardiovascular risk. To obtain odds ratios for these, the analysis was re-run with these replacing total cardiovascular risk.

NSAIDs = nonsteroidal antiinflammatory drugs.

complaints by subject or informant[28]) is consistent with that used in other research studies.[25] The subjects were not given detailed assessments by psychogeriatricians because this was impractical in the preoperative setting. No standardized method to assess subjective decline in memory currently exists, but the method used here is consistent with that used in other studies.[29]

Amnestic mild cognitive impairment represents an early manifestation of AD.[30] The construct of aMCI has evolved to identify subjects before they experience progression to AD. It is believed that once identified, these subjects may be amenable to treatment or prevention before overt dementia ensues, although to date, intervention studies in this regard have been somewhat disappointing. The prevalence of aMCI in the general community ranges from 14 to 18% in individuals 70 y or older, although this percentage changes according to variations in diagnostic criteria.[25] More importantly, individuals in the community with aMCI are likely to experience progression to dementia at a rate of 10–15% per year (the progression rate is higher in memory disorder clinics and patients attending AD centers).[25] There is evidence that subjects with aMCI already have AD pathology.[31] Dubois *et al.* proposed that the presence of an early and significant episodic memory impairment (reported by patients or informants), either isolated or with other cognitive changes and with objective evidence, constitutes a core diagnosis feature for the early detection of AD.[32] In this regard, the delayed recall of the CERAD AVLT is believed to be of importance because it represents the inability to encode, a key aspect of AD. In this study, the delayed recall of the AVLT displayed the greatest decrease of all the tests (compared with norms), underscoring the key part played by delayed memory in identifying aMCI.

The prevalence of aMCI reported in the current study is comparable with that of population studies of subjects not undergoing surgery. Indeed, there is little reason to believe that the prevalence in elective THJR surgery subjects should differ from the population at large, although it is possible these subjects may be more susceptible to cognitive decline because of inability to exercise.[33] By the same token, the population conversion rate to dementia of 10–15% per year[25] would indicate three to four of the aMCI subjects will experience progression to dementia per year, independent of any possible influence of anesthesia and surgery. However, there is evidence anesthesia and surgery may exacerbate the pathologic mechanisms of AD, which potentially could augment this conversion rate.[10,11]

The construct of PreCI has been investigated within the field of anesthesia in relation to identifying POCD after anesthesia and surgery. For example, memory has been mostly quantified using immediate recall, but it is now believed that encoding memory (assessed by delayed recall) is more indicative of AD. Few attempts have been made to relate POCD or PreCI to the onset of dementia in the longer term. This is unfortunate because recent animal studies suggest an association between cognitive change after anesthesia and the pathophysiology of AD[10,34]; however, this link has not been shown in clinical studies. The wealth of data outlining the progression of aMCI to dementia in population studies cannot be applied to PreCI because of the discrepancy in definitions between the two constructs.

To identify whether the process of anesthesia and surgery increases the rate of dementia in subjects who present with cognitive impairment, long-term follow-up will be required after subjects have been classified with aMCI. Such prospective trials would provide definitive evidence for an effect of

anesthesia and surgery on exacerbating AD. The prognostic information pertaining to aMCI cannot be applied to PreCI because the two constructs identify different cognitive properties, such that only 33% of the PreCI subjects were classified as having aMCI.

Silverstein *et al.*[12] established a surrogate measure of aMCI in subjects 60 y or older presenting for noncardiac surgery (comprising major abdominal and thoracic surgery in addition to orthopedic surgery), which they termed *preoperative cognitive impairment*. They defined this as impairment in cognition of more than 1.5 SD below healthy controls on immediate or delayed recall measures from the Visual Verbal Learning Test. They did not assess subjective memory complaints. Using this approach, they found an incidence of memory impairment of 6.2% (74 of 1,185 subjects) in their noncardiac group. The current study used similar criteria and found memory impairment in 76 of 152 (50%) subjects. It should be noted that Silverstein's group used the Visual Verbal Learning Test, whereas we used CERAD AVLT, which is an auditory, rather than a visual, test. It is unlikely that the visual, rather than auditory, presentation of words to be remembered would account for the large difference in results. The inclusion of subjects having nonorthopedic surgery is unlikely to account for such a large discrepancy. We can find no explanation for the discrepancy.

Multivariable regression identified age and pain as independent associations with PreCI and total cardiovascular risk factors and depression as independent associations with aMCI. Age and intelligence quotient have been repeatedly associated with POCD.[1,2] The lack of an independent association of age with aMCI is most likely the result of the low prevalence of aMCI (in 34 of 152 [22%] subjects), so the study may have been underpowered to detect such an association. It should be noted that the regression model used in this study was exploratory to identify associations between types of baseline cognitive impairment and patient demographic and risk factor variables. It was not a prediction model.

In conclusion, 20% of elderly subjects presenting for elective THJR surgery exhibit PreCI. The prevalence of aMCI in these subjects was 22%, which is commensurate with similarly aged individuals in the wider community. Differing objective criteria and the requirement for subjective complaints accounted for a small overlap between constructs. Future studies that track cognition before and after anesthesia and surgery should document the presence or absence of aMCI so that the rate of conversion to AD after anesthesia and surgery can be compared with that of the nonsurgical population.

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